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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,399	07/01/2003	John R. Desjarlais	067461-5097-US01	1891
67374 7590 06/20/2008 MORGAN, LEWIS & BOCKIUS, LLP ONE MARKET SPEAR STREET TOWER SAN FRANCISCO, CA 94105			EXAMINER EMCH, GREGORY S	
			ART UNIT 1649	PAPER NUMBER
			MAIL DATE 06/20/2008	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/611,399	DESJARLAIS ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 26 March 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 17, 18, 20, 22-25, 36, 37 and 39-45 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 17, 18, 20, 22-25, 36, 37 and 39-45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Response to Amendment***

Claims 17, 18, 22, 25, 39-42 and 44 have been amended, and claims 26 and 38 have been canceled as requested in the amendment filed on 26 March 2008. Following the amendment, claims 17, 18, 20, 22-25, 36, 37 and 39-45 are pending in the instant application.

Claims 17, 18, 20, 22-25, 36, 37 and 39-45 are under examination in the instant office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

### ***Claim Objections***

Claims 17, 36 and 37 are objected to because of the following informalities: claim 17 is missing a conjunction, i.e. "and," between parts a) and b). Appropriate correction is required. It is noted that amending claim 17, line 6 to include "and" after "Small Domain;" would be remedial.

### ***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39-43 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 39-43 depend from canceled claim 38, and claim 45 depends from canceled claim 26; thus, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of claims 39-43 and 45.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 17, 18, 20, 22-25, 36, 37 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Loetscher et al. (J Biol Chem. 1993 Dec 15;268(35):26350-7).

In the reply filed on 26 March 2008, Applicants assert that the Loetscher et al. reference "is the journal publication of US. Patent No. 5,597,899 to Banner, Lesslauer, Loetscher & Stuber ('the '899 Patent'), collectively 'Loetscher,'" and Applicants' arguments are presented with respect to the '899 Patent. Accordingly, it is noted that the Loetscher et al. reference of record (the J Biol Chem article) is not the same disclosure as the '899 Patent. Thus, Applicants' arguments are largely moot because

they refer to the disclosure of the '899 Patent and not to the disclosure of the prior art of record. Applicants are advised to refer to the prior art of record specifically when addressing outstanding prior art rejections. Regardless, the Examiner will attempt to address some of Applicants' arguments that may pertain to the prior art reference of record.

Applicants state that "Loetscher was attempting to identify human TNF muteins having higher binding affinity for human p75-TNF receptor than for human p55-TNF receptor and to specifically activate the p75 receptor" (Emphasis omitted). Applicants also state, "Moreover, Loetscher was in the context of using a TNF- $\alpha$  variants to kill tumors cells, and thus the variants MUST retain activity to at least one cognate receptor in order to kill tumor cells. This activity is opposite of the activity presently claimed herein. In the instant invention, the variant TNFSF does not activate any cognate receptor; nor does the variant TNFSF member of the present invention have receptor selectivity."

Applicants' arguments have been fully considered and are not found persuasive. Although the Examiner believes that Applicants are referring to the '899 Patent and not the prior art of record, it is irrelevant what "Loetscher was attempting to identify." Similarly, it is irrelevant whether the '899 Patent "was in the context of using a TNF- $\alpha$  variants to kill tumors cells." The instant claims are directed to products and not to methods. Therefore, as long as the prior art of record teaches a product(s) that meet(s) the limitations of the claims, the reference is a proper anticipatory reference. Applicants' assertion that in the instant invention, the variant TNFSF protein "does not activate any

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cognate receptor; nor does the variant TNFSF member of the present invention have receptor selectivity" is inaccurate. Claim 17 recites "wherein said mixed TNFSF oligomer has at least a 50% decrease in receptor activation as compared to a homotrimer of said wild-type TNFSF oligomer." Claim 18 recites "wherein said mixed TNFSF oligomer is substantially incapable of causing receptor activation as compared to a homotrimer of said wild-type TNFSF oligomer." Broadest reasonable interpretation of these limitations is that the claims encompass variant TNFSF proteins with at least 50% decrease in activation of just one receptor (in claim 17) and nearly a 100% decrease in activation of just one receptor (in claim 18). Thus, a prior art variant that has at least 50% decrease (or 100%) in receptor activation to at least one of the receptors would meet the limitations referred to above. Accordingly, the Loetscher et al. mutant R32W-S86T, for example, is taught to have "completely lost its binding affinity for TNFR-p75 but retained virtually all the binding activity for TNFR-p55" (p.26352, col.2, final paragraph). This mutant has at least one substitution in the Large Domain and at least one substitution in the Small Domain or the DE Loop as required by the claims and is substantially incapable of causing receptor activation (of one receptor), thus meeting the limitations of the claims. Therefore, the rejection is properly maintained.

### ***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregory S. Emch/

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Patent Examiner  
Art Unit 1649  
18 June 2008

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Primary Examiner, Art Unit 1646